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Analytics for Non-invasive Skin Imaging and Actinic Damage

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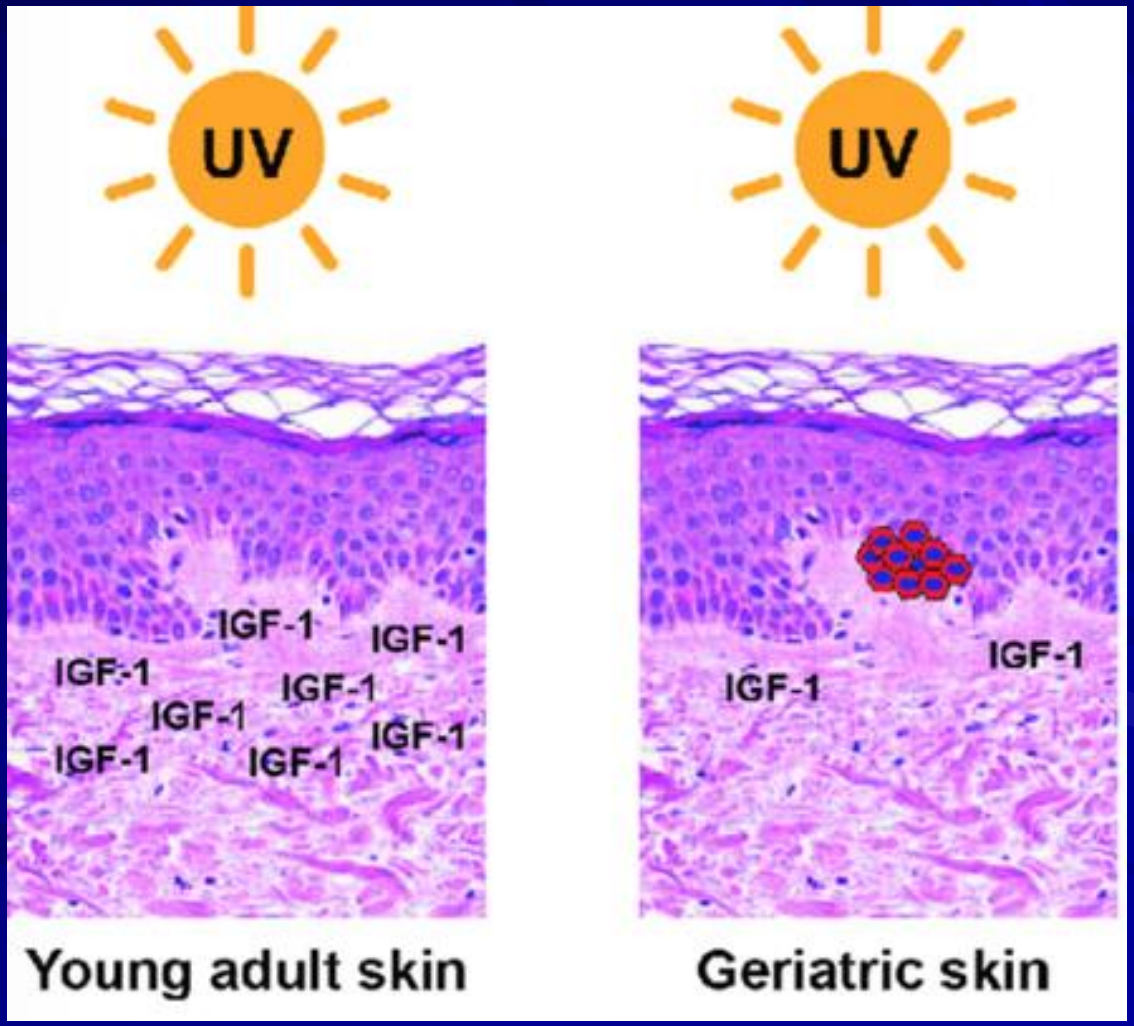
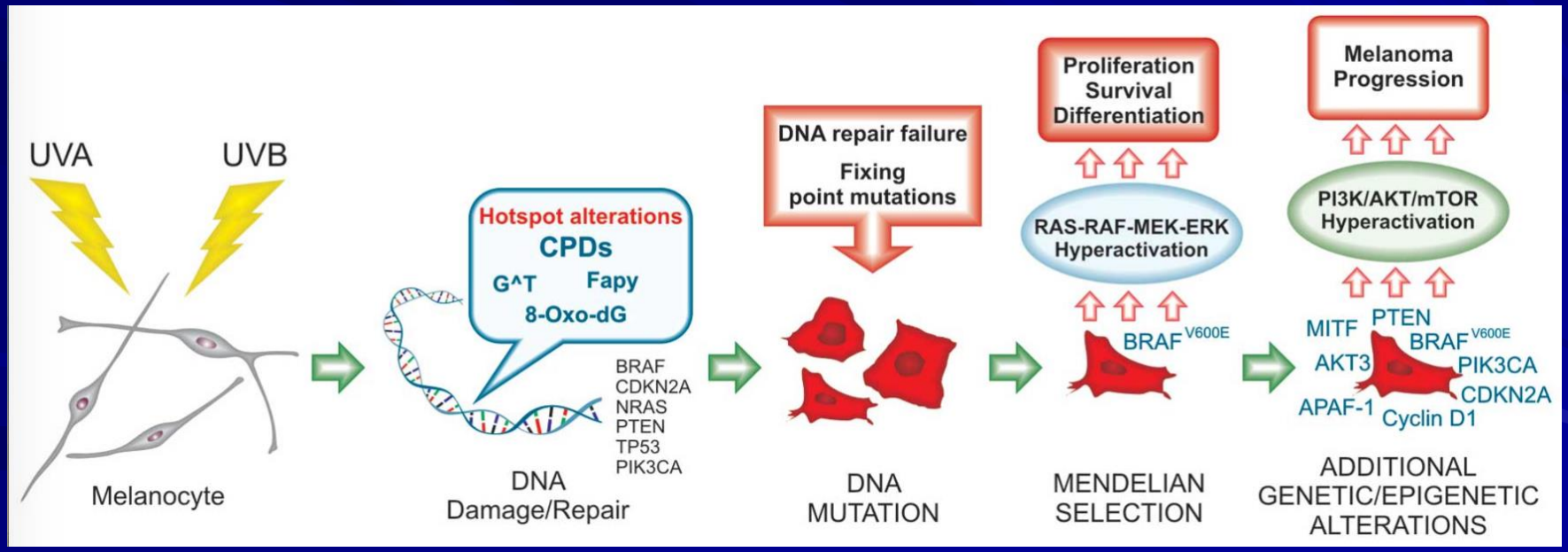
Elderly vs. Young Skin



Introduction

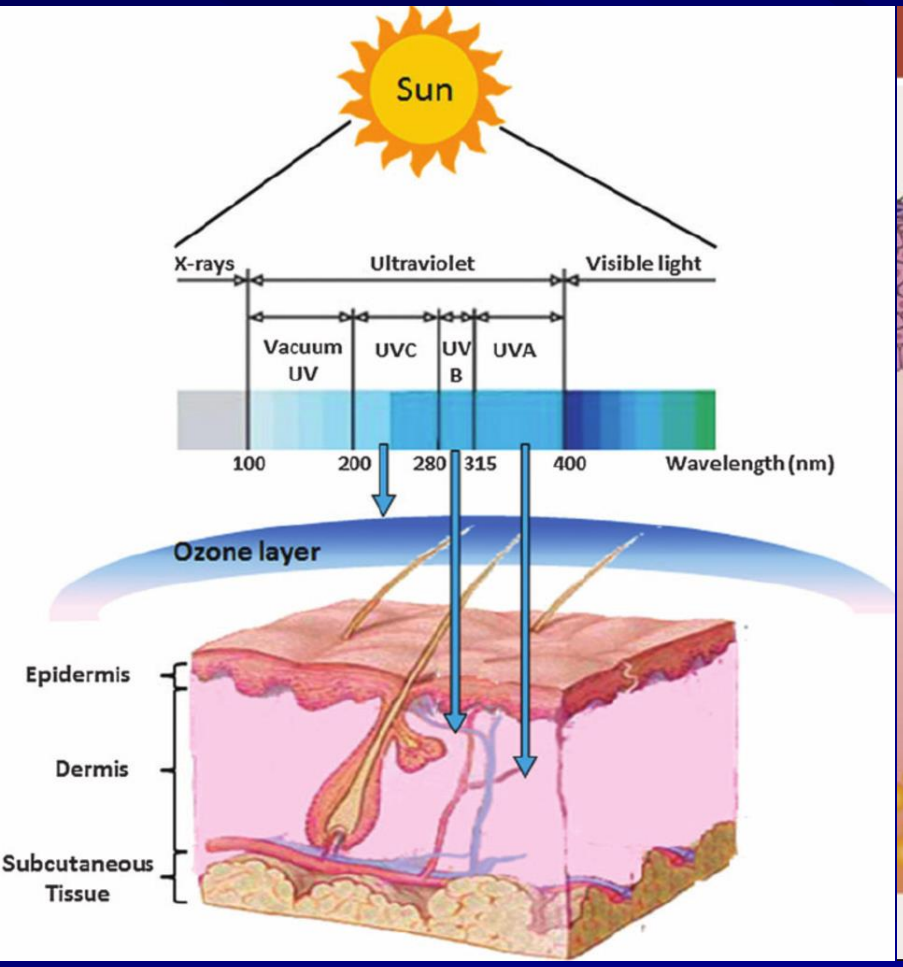
- **UVB Exposure**
  - Precancerous actinic keratoses are one of the most common abnormal growths due to UVB exposure
  - Upon damage, the keratinocytes develop mutations that can lead to cancer if left in the proliferating state

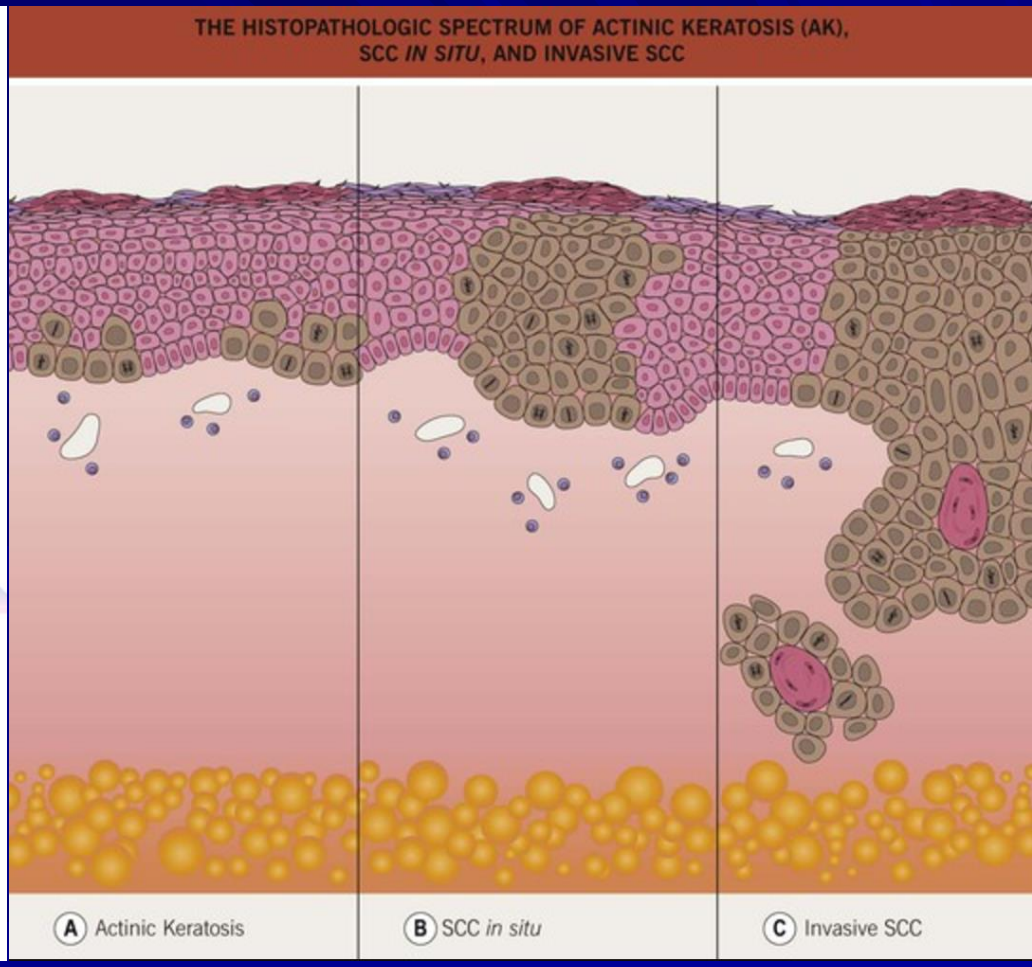


Introduction

- **Actinic Keratosis**
  - Identified by its crusty, scaly growth, reaching up to 1/8-1/4"
  - More than 419,000 cases in the U.S. each year linked to indoor tanning
  - Predominantly in elderly patients with fair skin
  - Usually found on the face and back of hands

AK can develop into squamous cell carcinoma





Clinical Importance

- **The Treatment of Actinic Keratosis**
  - The average annual cost to treat non-melanoma skin cancers is 5 billion dollars, which significantly impacts our healthcare system
  - In order to decrease morbidity and mortality rates in the early stages of the pre cancerous lesion, physicians must diagnose and begin treatment early
  - The goal is a non invasive and safe way to accurately measure the progress and severity of AK

Spatial Frequency Domain Imaging (SFDI).

- SFDI is a wide-field, non-contact mesoscopic optical imaging modality that can provide multiple parameters concurrently.
- In reflectance mode, it can provide maps of optical properties (absorption and scattering) and vascular parameters (hemoglobin concentrations and tissue oxygen saturation)
- Previous studies have shown it can be used to identify basal cell carcinoma skin cancers.
  - Academic Radiology 21: 263-70, 2014

Research Objectives

1. **Does non-invasive imaging of the skin have a clinical role in detecting and monitoring precancerous (AK) skin cancers?**
   -As shown in mice models, non-invasive imaging “hot spots” can correlate levels of hemoglobin in areas of the skin after UVB treatments
   -We wanted to bring this discovery to patients in the clinical setting

2. **Can SFDI imaging measurements and parameters be implemented as biomarkers of neoplasia?**
   -To better plan intervention treatments and for accuracy in diagnosis, it is necessary to predict the level of cancer progression
   -Optical imaging techniques can drastically improve the early stages of disease, and outcomes
   -Ideally SFDI will be used for frequent monitoring of the at risk precancerous populations

Methods

- **Clinical Trial**
  - We initiated an IRB approved clinical trial at Wright State Physician's Pharmacology Translational Unit
  - 55 test subjects over the age of 35 years with fair skin (Fitzpatrick scale I or II) with no subjects having history of tanning bed/chronic UVB exposure
  - The subjects all expressed different levels of photodamage, especially actinic keratosis
  - Wide field photograph images were taken of both subject's arms from their elbow to knuckle to be diagnosed by Dermatologists
  - Three 3cm X 4cm areas of each arm was also captured to be analyzed by SFDI

Methods

- **SFDI**
  - The wide field, non contact machine gathers data on the basis of multiple parameters: reflectance mode, vascular mode, and fluorescence imaging mode
  - Maps of absorption and scattering, hemoglobin concentrations, and tissue oxygen saturation were graphed for each subject's arm
  - The Engineering Department analyzed results using a custom MATLAB software to fit data at each pixel

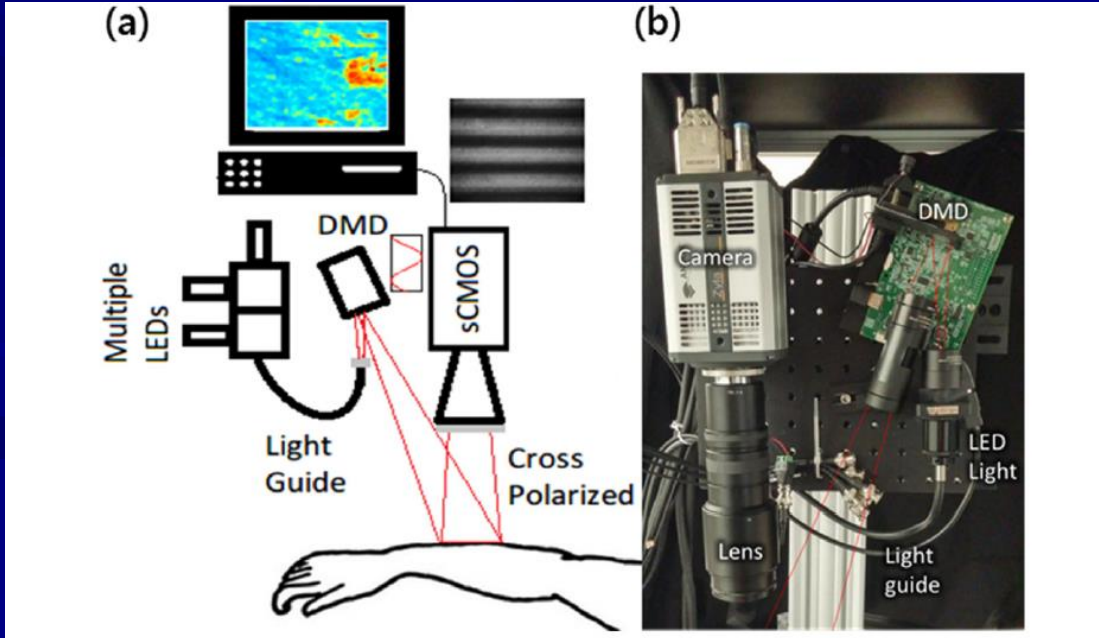


Fig. 2. (a) Schematic diagram and (b) photo of SFDI instrument for imaging lesions on arm.

Methods

- **Dermatologist scoring criteria**
  - 15 Dermatologists rated each photograph according to the Global Assessment Severity Scale via McKenzie et al publication scoring guidelines
  - The physicians rated each forearm from 0-9, including duplicate images to maintain and measure levels of consistency
  - The scoring ranged from 0 (less severe) to 9 (the most progressed stage of skin damage)

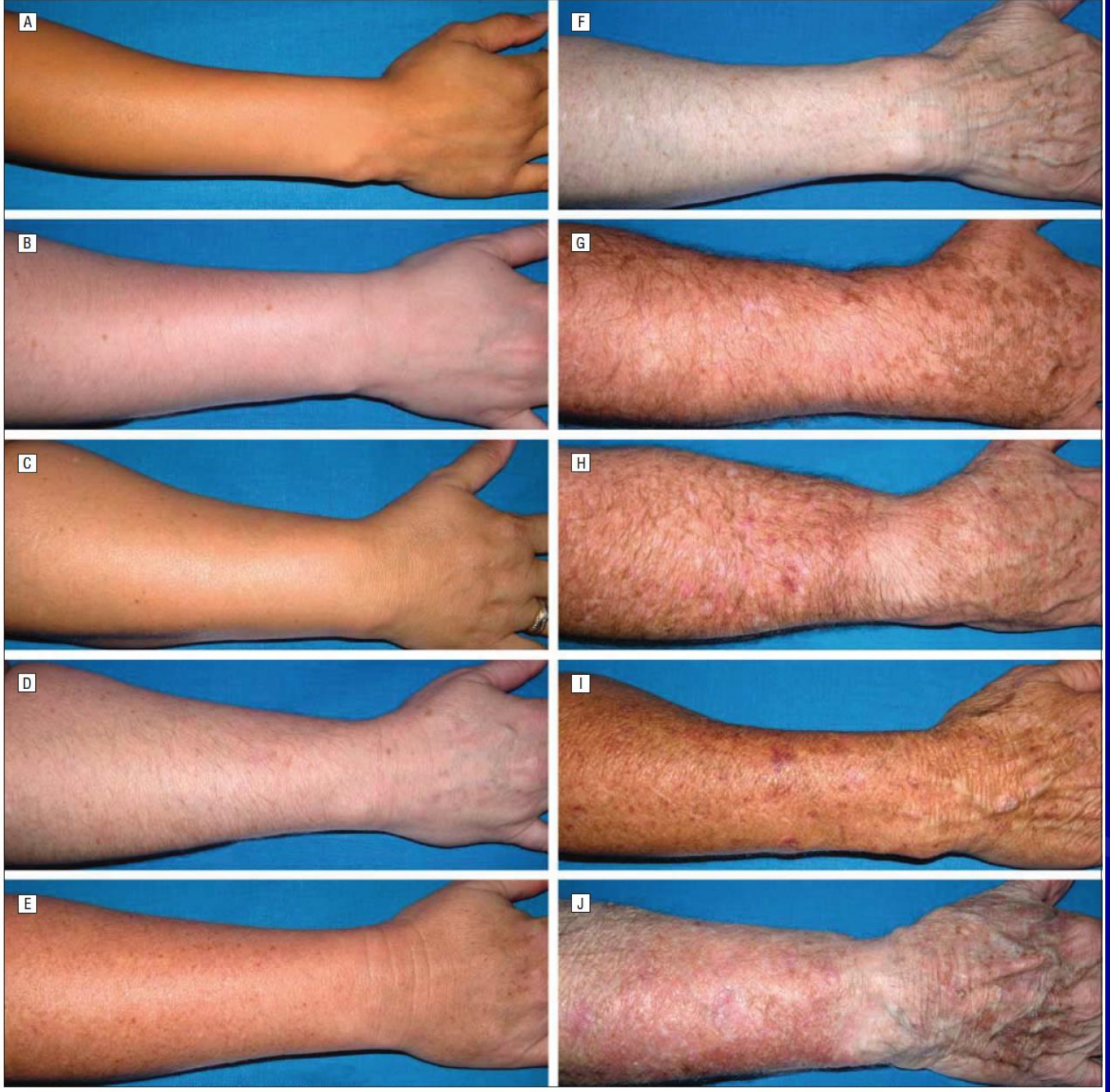
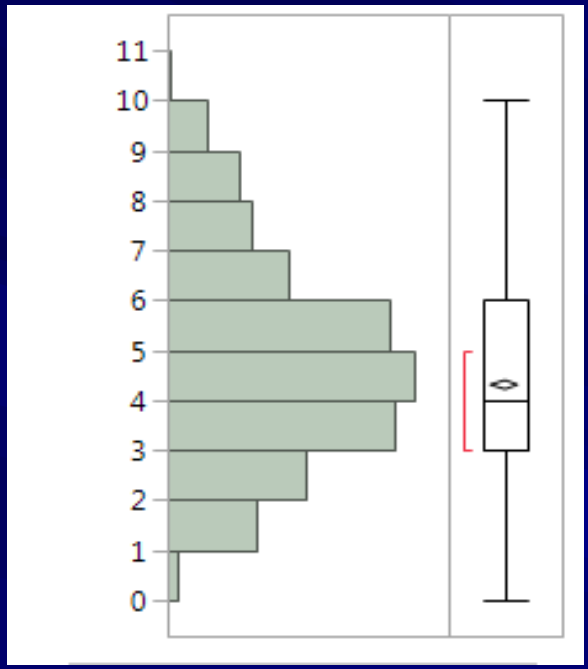


Figure 3. Global assessment: severity score 0 (A); 1 (B); 2 (C); 3 (D); 4 (E); 5 (F); 6 (G); 7 (H); 8 (I); and 9 (J).

Results

- **Can a relationship be obtained between Dermatology scores and Actinic Imaging?**



Few extreme scores were seen in the Dermatology data (Figure 1), but large ranges showed in individual scores (Figure 2). This poses the possibility that concordance between dermatologists was not always present.

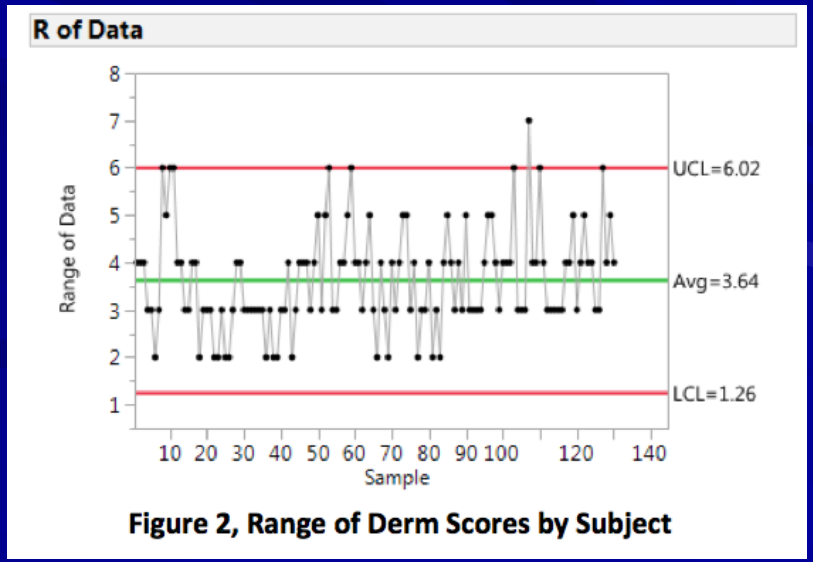


Figure 2, Range of Derm Scores by Subject

Analysis of Variance

- Three factors were considered for the ANOVA model of data analysis
- The patient is considered the most important of the variables, but the dermatologist evaluation of the patient is also a statistically significant predictor of score
- A second opinion from other dermatologists can therefore provide a different diagnosis
- This is consistent with the ANOVA Table seen below:

ANOVA Table for Dermatologist, Arm, and Patient in Relation to Dermatologist Score

Source		DoF	Sum of Squares	Mean Squares	F-Ratio	p
Model		69	6314.11	91.51	93.08	<0.0001
	Dermatologist	14	739.86	52.85	53.75	<0.0001
	Patient	54	5567.96	103.11	104.88	<0.0001
	Arm	1	2.68	2.68	2.73	0.09
Error		1880	1848.31	0.98		
Total		1949	8162.43			

Conclusion

- **SFDI Mapping**
  - SFDI can provide quantitative maps along the parameters of optical and vascular modes to classify precancerous lesions in humans
  - Actinic keratosis stage can be correlated to levels of scattering and hemoglobin concentration
  - Further analysis will be done of the different parameters and values gathered simultaneously from each subject arm section to decide which are most indicative of AK stage
- **Dermatologic Analysis**
  - The Dermatologist scores, 0-9, showed patterns of least and most progressive stages of skin damage, with greatest variance on the middle scores/more subjective diagnoses
  - Further methods to find the best statistical model will be explored, along with different types of criteria to correlate the SFID results

Current Work

- Create algorithm to classify actinic damage score based on mesoscopic imaging
  - Ground truth hard to determine due to dermatologist disagreement
- To use SFDI to map skin and conduct skin biopsies to examine IGF-1 levels in “hot spots” vs “cold spots”.
- To compare skin before or after a “field therapy” such as topical 5-fluorouracil for changes in SFDI parameters.

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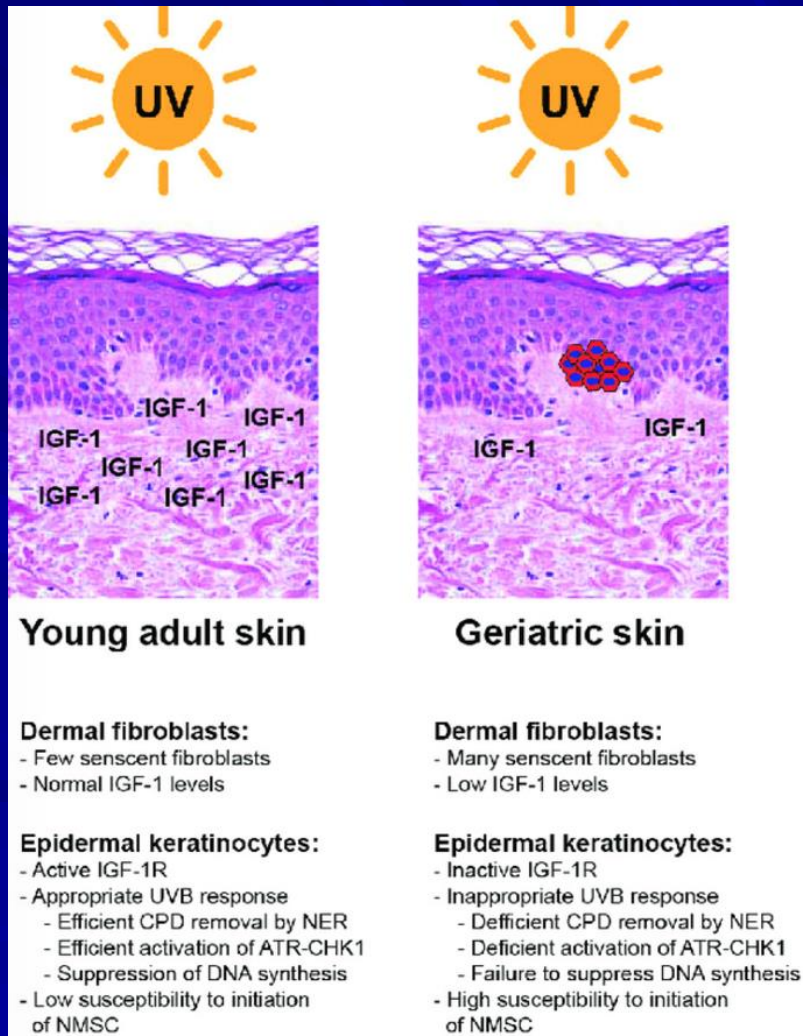
Age's Effect on Skin Cancer

- **Insulin-like Growth Factor 1 (IGF-1)**
  - Skin Cancer incidence rates increase with patient age
  - Our lab has previously found that elderly skin does not produce as much IGF-1 as younger skin
  - Activation of IGF-1 on keratinocytes induces senescence after UVB exposure, to prevent damaged cell proliferation
  - Elderly skin is linked closely with senescent fibroblasts located in the dermis layer of skin
  - Since the fibroblasts are responsible for producing IGF-1, the protein is downregulated in elderly dermis
  - Our past in vitro studies have proven that when the keratinocytes are treated with UV radiation without IGF-1, these damaged cells will uncontrollably proliferate

Future:

- To use SFDI to map skin and conduct skin biopsies to examine IGF-1 levels in “hot spots” vs “cold spots”
- To compare skin before or after a “field therapy” such as topical 5-fluorouracil for changes in SFDI parameters



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